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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/121,017	07/22/1998	TORU IMAMURA	382.1019	2849

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DAVIDSON, DAVIDSON & KAPPEL, LLC
485 SEVENTH AVENUE, 14TH FLOOR
NEW YORK, NY 10018

EXAMINER	
SAUNDERS, DAVID A	
ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 01/10/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/121,017	IMAMURA ET AL.	
	Examiner	Art Unit	
	David A Saunders, PhD	1644	

-- The MAILING DATE of this communication appears on the cover sh et with th correspond nce address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 September 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-6,14,18-21 and 23-37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-6,14,18-21 and 23-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/7/04 (i.e. an amendment and an IDS) has been entered.

Following entry of the amendment of 9/7/04, claims 1, 3-6, 14, 18-21, and 23-37 are pending and under examination.

The specification is objected to because of the following informalities: At page 10, line 23 there is a pentapeptide, which is not identified with a SEQ ID No. This sequence does not appear with an identifying SEQ ID NO. in the sequence listing. Applicant must provide a SEQ ID No to identify thus sequence or to identify the residues of an already listed SEQ ID NO that would identify this pentapeptide. Full compliance with 37 CFR 1.821-1.825 is required. Appropriate correction is required.

The amendment of 9/7/04 has overcome 112 first and second paragraph rejections of record except as stated infra.

Claims 1, 3-6, 14, 18-21 and 23-27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 1, 3-6, 18-21 and 23-27 "activity" is unclear, because one does know whether this refers to the heparin – binding activity or another activity (e.g. the growth promoting activity of FGF.

The examiner notes that deletion of the modifier "residual" before "activity" does not overcome the ambiguity in the meaning of "activity" per se.

Claim 1 is confusing by reciting, in the concluding lines, "wherein the heparin binding protein comprises the amino acid sequence of SEQ ID NO: 1, 17, 19, 21, 23 or 29." As the examiner understands the disclosure and the sequence listing, SEQ ID NO: 1, 17, 19, 21 and 23 consist of a part of human ryudocan fused to a part of human FGF-1, with the latter being "the heparin binding protein" portion of the fusion protein. Likewise SEQ ID NO: 29 consists of mouse FGF-6, human FGF-1 and an "artificial sequence. Since the proteins comprising the sequences recited in claim 1 have more than a "heparin binding protein" portion, it appears that applicant could more properly conclude with a recitation of - - wherein the functionalized heparin binding protein comprises the amino acid sequence of SEQ ID NO: 1, 17, 19, 21 or 29. - -. A like consideration applies to independent claims 18-20 and 23.

Claims 4 and 18-20 each fail to clearly set forth the relationship between the "peptide" (i.e. at claim 4, line 2; claim 18, line 3, etc.) and the recited SEQ ID NOS. From the disclosure, the examiner considers that the "peptide" to which the sugar chain(s) is covalently bonded is a segment within each of SEQ ID NOS: 1, 17, 19, 21, 23 and 29. That is to say, the ryudocan segment at the N-terminal of SEQ ID NOS: 1, 17, 19, 21 and 23 would constitute the "peptide" to which the sugar chain(s is covalently bonded; likewise the "artificial sequence" within SEQ ID NO: 29 may be the "peptide" to which the sugar chain(s) is covalently bonded.

Claim 19 is confusing as to where, within the functionalized heparin binding protein, the sugar chain is covalently bonded. Recitation of "a heparin binding protein and a plurality of sugar chains covalently bonded thereto "(lines 1-2) can include bonding of the sugar chains directly to an amino acid of the heparin binding protein, per se; however, it appears that, lines 6-7 require the sugar chains to be covalently bonded to another peptide.

New claim 30 has an improper Markush group starting at line 6. Five members are recited, each member being a particular segment of a different SEQ ID NO. Each segment, however, has the same number of residues (134) and the same sequence, when they are all aligned. Part (b) of claim 30 therefore properly has only one member.

Claims 3, 20 and 31-33 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 3 does not further limit base claim 1, which as noted supra, recites six SEQ ID NOS, all of which have a human FGF-1 segment. Therefore recitation in claim 3 of "belonging to the FGF family" adds no further defining limitation that is not inherent to base claim 1.

For like reason claim 21 fails to further limit claim 20.

Since the segments of the SEQ IDS NOS recited in claim 30 all correspond to the human FGF-1 sequence within each SEQ ID NO, claims 31-33 fail to further limit claim 30.

Claims 4-5 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 4 does not further limit claim 1 by reciting "to a peptide, which is covalently bonded to the heparin binding protein".

It is noted that claim 1 has been amended to recite at set of SEQ ID NOS. as for as the examiner can discern from the sequence listing of 6/27/00, SEQ ID NOS: 1, 17, 19, 21 and 23 are each fusion proteins of a part of human ryudocan and a part of human FGF-1 in which the ryudocan domain has the site(s) for covalent sugar chain bonding. SEQ ID NO: 29 are a fusion protein of a part of mouse FGF-6 (serving as a signal sequence), a part of human FGF-1, and "an artificial sequence" (serving as a domain for covalent sugar chain bonding?). Since these are fusion proteins the peptide (e.g. ryudocan) to which the sugar chain(s) is covalently bonded is inherently "covalently bonded" (through a peptide bond) to the heparin binding protein.

By reciting "covalently bonded" in claim 4, applicant has added no feature that is not inherent to the proteins of base claim 1.

Further dependent claim 5 is objected to for the above reason and, also, because it recites (least line) "the peptide to which the sugar chain is added comprises a proteoglycan core protein or part thereof". As for as the examiner can determine from the sequence listing for SEQ ID NO: 29, there is an "artificial sequence" but no

"proteoglycan core" (e.g. ryudocan) within the SEQ ID NO: 29. Claim 5 would thus fail to properly further limit the embodiment of base claim 1 pertaining to SEQ ID NO: 29.

Claims 1, 3-6, 14, 18-19, 23-27 and 29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims contain new matter.

Claim 1 contains new matter at lines 1-2 by reciting "a heparin binding protein and at least one sugar chain covalently bonded thereto". If one interprets "thereto" as meaning that the sugar chain is covalently bonded to an amino acid residue within the sequence of the heparin binding protein, per se, then applicant is reciting new matter. As has been noted supra, the examiner considers that it has been disclosed that SEQ ID NO: 1, 17, 19, 21 and 23 contain a ryudocan domain, to which the sugar chain is to be covalently bonded. Likewise SEQ ID NO: 29, contains "an artificial sequence" domain to which a sugar chain is to be covalently bonded. It is noted that page 15 sets forth an embodiment in which the sugar – chain is to be covalently bonded directly to the heparin binding protein; this embodiment was, however, disclosed as being an alternative to, not as being in addition to the provision of a fused peptide domain for the addition of sugars, as one has in SEQ ID NOS: 1, 17, 19, 21, 23 and 29.

Claims 18-19 and 23 are rejected in like manner.

Claims 4-5, 18-21, 24 and 26-28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims contain new matter.

As has been noted supra the proteins of SEQ ID NOS: 1, 17, 19, 21, 23 and 29 inherently have a segment (e.g. ryudocan) which has been disclosed as the segment to which the added sugar chains will become covalently bonded.

If one interprets the "peptide, which is covalently bonded to the heparin binding protein" of claim 4 to be a peptide other than that inherently present in SEQ ID NOS: 1, 17, 19, 21, 23 and 29 for the covalent binding of the sugar chain(s), then applicant has added new matter. The examiner finds no original disclosure of a functionalized heparin binding protein that has two different peptide segments covalently binded thereto for the purpose of adding covalently bonded sugar chains.

For like reason claim 18 is rejected, because it does not clearly require that the "peptide" (line 3) to be within the SEQ ID NOS: recited at the conclusion.

Claim 19 is rejected because it does not clearly require the "peptide" (line 7) to be within the SEQ ID NOS recited at the conclusion.

Claim 20 is rejected because it does not clearly require the "peptide" (lines 2 and 4) to be within the SEQ IDS NOS recited at the conclusion.

Claims 6 and 14 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 6 recites new matter by requiring the "at least one sugar chain" to be "bonded to the heparin – binding protein.

As noted supra, the examiner has understood that the sequence listing indicates that SEQ ID NOS: 1, 17, 19, 21 and 23 of base claim 1 have a fused ryudocan domain, to which the sugar chain is covalently bonded. Likewise SEQ ID NO: 29 of claim 1 has a fused "artificial sequence" to which the sugar chain is covalently bonded. The embodiments recited in dependent claim 6 were set forth at specification page 15 as pertaining to methods by which the sugar chain is added to the heparin - binding protein, per se, by a chemical method, as opposed to a method by which the sugar chain is added to a peptide sequence fused to the heparin binding protein. Applicant is thus claiming an embodiment of sugar chain addition that was not originally disclosed.

The amendment has overcome the previously stated 102(e) rejection over Saunders et al, who do not teach proteins of the SEQ ID NOS. recited in instant claims 1, 17, 19, 21, 23 and 29. Also Saunders et al do not teach the particular sequence of FGF-1 recited in part (b) of claim 30.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Saunders whose telephone number is (571) 272-

0849. The examiner can normally be reached on Monday to Thursday from 8 AM to 5:30 PM and on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Saunders/LR
December 20, 2004

David A Saunders
DAVID SAUNDERS
PRIMARY EXAMINER
ART UNIT ~~182~~ 1644